REMARKS

Status of the Claims

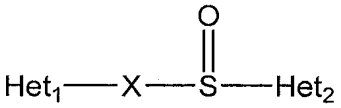
Claims 1-6 and 9-21 are pending, with claim 1, 16 and 17 being independent. Claims 19-21 have been added. Support for the claim amendments can be found throughout the specification, e.g. pages 6-8. Therefore, no new matter has been added.

Applicant respectfully requests the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and the following remarks.

Rejection under 35 U.S.C. § 103(a)

Claims 1-6 and 9-18 are rejected under 35 U.S.C. § 103(a) in the Final Rejection as allegedly being unpatentable over U.S. Patent No. 6,730,685 (Brulls) in view of Facts and Comparisons.

Brulls discloses stable water free liquid formulations for acid labile benzimidazole compounds, such as proton pump inhibitors (PPIs). Brulls discloses formulating the sodium or potassium salts of compounds having the general formula:



All of the examples in Brulls are directed to formulations of the sodium salt of omeprazole, which comprise polyethylene glycol (PEG).

The Office Action alleges that "Brulls teaches pharmaceutical compositions that are combinations of tenatoprazole and H_2-blockers, such as ranitidine. See column 7, lines 22-26."

Applicants respectfully submit that Brulls does not disclose or suggest pharmaceutical compositions that are combinations of specifically tenatoprazole and H_2-blockers, such as ranitidine. The cited portion of Brulls (column 7, lines 22-26) is shown below.

> The formulations may also be used in combination with other drug treatments, such as one or more antibacterial compounds, a motility stimulating drug, an antacid and/or a H_2 -blocker, such as for instance ranitidine.

Applicants submit that the statement in Brulls that "[th]e formulations may also be used in combination with other drug treatments" is meant to encompass that a person may

take a dose of the formulation of the proton pump inhibitor and may also take a ***separate dose*** of another drug treatment. Applicants further respectfully submit that the phrase in Brulls that "the formulations may also be used in combination with other drug treatments" is **not** a teaching that the compositions are "combinations of tenatoprazole and H_2-blockers", as alleged in the Office Action. Applicants respectfully submit that one of ordinary skill in the art would not interpret Brulls as disclosing or suggesting combining tenatoprazole and H_2-blockers into a single composition.

The document "Facts and Comparison" relates to ranitidine and provides information on dosing, pharmacokinetics and indications of use. However, this document does not disclose or suggest the combination of tenatoprazole with H2-receptor antagonists.

Applicants respectfully submit that Brulls provides a general description of ***all*** PPIs and does ***not*** specifically name tenatoprazole. In fact, Brulls focuses on omeprazole (See examples). Applicants respectfully note that the present invention is not directed to a combination of a H2-receptor antagonist with ***any*** PPI, but with tenatoprazole specifically. Applicants respectfully submit that in no way does Brulls disclose or suggest the presently claimed combination of ***specifically*** tenatoprazole with a H2-receptor antagonist.

As described above, the document "Facts and Comparison" merely relates to ranitidine and provides information on dosing, pharmacokinetics and indications of use. Accordingly, as presently cited, Applicants respectfully submit that the document "Facts and Comparison" fails to cure the above-described deficiencies of Brulls. Therefore, even if combined, Brulls and the document "Facts and Comparison" do not disclose or suggest the presently claimed combination of ***specifically*** tenatoprazole with a H2-receptor antagonist.

Moreover, Applicants respectfully submit that the combination of tenatoprazole with H2-receptor antagonists provides results that were not expected based what was known or expected from other members of the PPI family of compounds. The instant specification states:

> On the contrary, the studies performed by the applicant have shown that the combination of a specific proton pump inhibitor, i.e. tenatoprazole, and a histamine H2-receptor antagonist procures unexpected effects which compared with other proton pump inhibitors and other histamine H2-receptor antagonists, used alone or in combination. More particularly, it has been shown that the combination of tenatoprazole and one or more histamine H2-receptor antagonists enables control of gastric acidity which is markedly superior to that achieved with each of the components used alone, and particularly allows the effective treatment of patients suffering from

symptoms and lesions related to gastroesophageal reflux and refractory to standard therapy with a proton pump inhibitor. (See page 3, lines 7-19)

Furthermore, on pages 8 and 9 of the specification, the treatment of patients with symptoms of gastroesophageal reflux is discussed. The treatment was with tentaprazole and ranitidine. The results of the study showed great safety and favorable evolution of the symptom.

Accordingly, Applicants respectfully submit that the claimed combination of specifically tenatoprazole and a histamine H2-receptor antagonist provides unexpected results compared to what was known, or would have been expected from other PPIs.

Moreover, Applicants respectfully submit that there is no suggestion or motivation in either Brulls or Facts and Comparisons to combine specifically tenatoprazole and a histamine H2-receptor antagonist into a composition, as required by the present claims. One of ordinary skill in the art, upon reading Brulls, would not be motivated to combine specifically tenatoprazole and a histamine H2-receptor antagonist into a composition for at least two reasons. First, Brulls explicitly discloses that there are significant stability problems with PPIs. Brulls is directed to a method of overcoming the instability of PPIs by forming a specific composition that provides increased stability of PPIs. Brulls also discloses that formulations of a PPI may be used in combination with other drug treatments, not that other active ingredients may be combined in the formulation of Brulls. Therefore, one of ordinary skill in the art would be motivated by the teachings of Brulls not to develop a composition comprising tenatoprazole and a histamine H2-receptor antagonist such as ranitidine.

The Office Action has not provided any suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Applicants respectfully submit that there would not have been a suggestion or motivation in Brulls and the document "Facts and Comparison" or the knowledge generally available to one of ordinary skill in the art, to modify the reference to obtain the Applicants' invention.

Moreover, Applicants respectfully submit that there is no reasonable expectation of success in the combination. The specification of the instant application (page 2, line 26 - page 3, line 6) describes the results of studies reported by PL Peghini et al. (Gastroenterology, 1998) and LB Cross et al. (Ann. Pharmacother., 2002) that investigated various treatment regimes where ranitidine and omeprazole where administered at different

times of the day. As indicated in the specification, there did not appear to be an advantage in a combination treatment of omeprazole (a PPI) and ranitidine (a H_2-receptor antagonist). Such teachings would not lead one of ordinary skill in the art to make the combination of a proton pump inhibitor and a H_2-receptor antagonist. In fact, such a teaching would teach-away from such a combination.

Because the claims of the instant application require tenatoprazole, a specific PPI, there is even less likelihood that one would choose this specific PPI to use in combination with an H_2-receptor antagonist, when the prior art teaches against the combination with the most widely used member of the family of PPIs. It is only through the knowledge gained by reading the instant specification that one of ordinary skill in the art would select tenatoprazole from among the various PPIs to combine with a H_2-receptor antagonist, especially when the prior art teaches away from such a combination. Therefore there would not be a reasonable expectation of success in obtaining the applicants' invention by modifying the cited prior. And, as shown in the study discussed on pages 8-9 of the specification, the combination of tentaprazole and ranitidine works.

Therefore, in light of at least the foregoing, Applicants respectfully submit that claims 1-6 and 9-18 are not obvious over Brulls in view of Facts & Comparisons and these claims are allowable. Accordingly, Applicants request that the rejection of these claims should be withdrawn.

Conclusion

For the reasons noted above, the art of record does not disclose or suggest the present claims.

In view of the foregoing amendments and remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time. Please charge any deficiency in fees or credit any overpayment to Deposit Account No. 05-1323 (Docket # 104006.B130119).

Respectfully submitted,

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By: _____
E. Joseph Gess
Registration No. 28510

Crowell & Moring LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-2500
EJG/gs